Influence Of Dexamethasone And Gamithromycin On The Acute Phase Response In LPS-Challenged Calves

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Introduction

Lipopolysaccharide (LPS) is a potent inducer of the bovine acute phase response and has been widely used in research to provoke acute inflammation. An intravenous challenge with LPS elicits the endogenous synthesis and release of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). These cytokines initiate fever and stimulate the hepatic production of acute phase proteins, such as Serum Amyloid A (SAA). Regarding the fact that immunomodulating drugs are able to influence this acute phase response, the aim of the present research was to study the potentials of dexamethasone and gamithromycin in a standardized LPS-inflammation model. Dexamethasone was applied as a positive control, due to its major anti-inflammatory effects. The novel azalide gamithromycin on the other hand, was selected since macrolide antibiotics have been reported to exert immunomodulatory effects. Furthermore, the combination of both drugs was studied for possible additive and/or synergistic effects.

Materials and Methods

A standardized and reproducible inflammation model was developed by challenging twelve 4-week-old calves intravenously with a single dose of LPS (*E. coli* serotype O111:B4, 0.5 µg/kg body weight (BW)). Three control animals on the other hand received an equivalent volume of 0.9% NaCl. Rectal body temperature was measured and plasma samples were collected at several points in time until 72h p.a. These samples were analyzed using ELISAs for TNF-α, IL-6 and SAA. As part of the immunomodulation study, eighteen different calves were randomly divided in three groups, each group consisting of six calves. The groups received a single bolus of respectively 0.3 mg/kg BW dexamethasone i.m. (Dexa 0.2%®, Kela), 6 mg/kg BW gamithromycin s.c. (Zactran®, Merial) and the combination of both drugs. At T_{max} of the drug (time at which the maximum plasma concentration is reached) the LPS-bolus was administered, followed by a similar experimental design as for the inflammation model.

Results and Conclusions

In comparison with the results obtained in LPS-administered animals which did not receive any treatment, dexamethasone and the combination of dexamethasone and gamithromycin significantly inhibited the release of TNF-α, IL-6 and SAA after an LPS-challenge. The administration of gamithromycin solely did not affect the cytokine and acute phase protein concentrations. Regarding the course of the body temperature, neither dexamethasone, nor the combination had a major influence, while gamithromycin alone induced a remarkable delay of the maximum body temperature. In other words, these results demonstrate the possible additive effect of a combined administration of an antibiotic with a corticosteroid in the acute phase of a bacterial infection, which could contribute to a better clinical condition of the animal.